REMARKS

The Applicants would like to thank the Examiner for the opportunity to meet on April 21, 2004 and discuss the pending issues in this continuation application. The Applicants also appreciate the Examiner's suggested claim revisions of May 12, 2004.

The Applicants have reviewed the Examiner's suggested claim and provided a new set of claims for the Examiner to review in this second preliminary amendment. The Applicants do not believe that a Jepson style claim is appropriate for the present invention. Applicants suggest that the present invention is not merely an improvement of solid phase peptide synthesis, but a novel method for synthesizing peptides of a particular size so that they are prepared as dimers (or trimers) having free c-terminal ends. The claimed invention is of particular use in antigen presentation where the c-terminal end of the antigen must be free to activate an immune response.

Claims 66-83 are cancelled, and claims 84-97 are newly presented. Support for the new claims can be found in the specification. No new matter has been added with this amendment. It is believed that the claim language now more clearly defines the invention.

With regard to claim 84 (corresponding to previously presented claim 66), Applicants propose adding a limitation of between 4 and 20 amino acids to the peptide sequence, and that the peptides have free c-terminal ends in the preamble. Applicants also point out that we have replaced

the term "ligand" with the term "peptide sequence" to more accurately describe the invention. In step (a), Applicants have rewritten this step to more clearly show where the starting peptide sequence originates from and how it is attached to the resin. For example, the composition is described as a formula $[H_2N\text{-}A\text{-}CO]_a\text{-}S$ to more clearly denote the starting structure of the synthesis. Applicants also deleted the term 'ligand' and substituted the term 'peptide sequence' for consistency.

Additionally, Applicants have added a new step (c) which distinctly defines the amount of dicarboxylic acid needed in the synthesis to be between 0.4 and 0.6 equivalents with respect to the free N-terminal amino groups. Step (c) was also amended to include specific dicarboxylic acids of the formula $R(COOH)_2$, and more clearly defines R as being $N(X)(CH_2\text{-})_2$, $NH(X)CH<$, $CH_2<$, $NH(X)CH(CH_2\text{-})_2$ or $CH_2(CH_2\text{-})_2$ group, and X represents an Fmoc, Boc or Aloc group and furthermore defines the product of the acidification as:

$$[H_2N\text{-}A\text{-}CO]_{a\text{-}b} > S$$

$$[HOOC\text{-}R\text{-}CO\text{-}HN\text{-}A\text{-}CO]_b, \quad \text{(Formula III)}$$

wherein b is between about 0.4a and 0.6a.

Applicants wish to show that the two new formulas III and IV (which are merely new schematics of what was previously presented) depict the reaction as a two-step process. As the Examiner may recall during our interview, the reason this process uses only achiral amino acids

(instead of chiral as used by Lange et al.) is because of this two-step process. The first step is slow, not because of difficult reaction kinetics, but because only half an equivalent of acid is used to react, while the second step is considered faster because the sequences are aligned for the cyclization reaction (to give formula IV).

Applicants also further defined the resulting ring structure in step (c) that is formed when the dicarboxylic acid groups link with the N-terminal amino groups of the peptide sequences attached to the solid-phase synthesis resin as:

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      CO-HN-A-CO
R<                >S
      CO-HN-A-CO      (Formula IV) .
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A limitation of linking via the N-terminal amino groups was added to address concerns the Examiner expressed regarding the Gilon reference.

Applicants would like to respectfully point out that after the interview, the Applicants reviewed the Gilon reference again and noticed that the diagram Applicants used in the interview was not accurate. Our depiction showed the Arg and Gly linked through a dicarboxylic acid by their side amino group and N-terminal groups respectively. This is not correct. As we have stated previously, the paper shows that Gilon does not use Gly but a modified Gly called N-(ώ-amino alkylene)Gly (Page 482). Therefore the Gilon construct is not linking two amino acids with free amino groups via a dicarboxylic acid, but

instead, linking a synthetic amino acid with an alkyl linker of 2, 3 or 6 methylene units.

Applicants point out that the present invention does not contain any such modified amino acids in the peptide sequences. Nor does the present invention teach or suggest that the peptide sequences are linked via alkyl linkers. Applicants suggest that such specifically modified amino acids would not normally be encompassed by the term "peptide sequence" as understood by those of skill in the art. Additionally, as we stated at the interview, the ring structure created is not a cyclization of the peptide sequences themselves with alkyl linkers, as in Gilon, but instead, they comprise a solid phase linked to a peptide sequence, linked to the dicarboxylic acid, linked to a second peptide sequence, which is then linked back to the solid phase. In claim 84, step (c) has been written to more clearly show the "ring" structure of the invention:

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      CO-HN-A-CO
   R<           >S
      CO-HN-A-CO    (Formula IV).
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Finally, claim 84 was drafted so that step e) defines an optional splitting of an N-terminal Fmoc-group, Boc-group or Aloc-group and step f) defines the cleavage step and the resultant product as:

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      CO-HN-A-CO-Y
   R<
      CO-HN-A-CO-Y ,          (Formula V),
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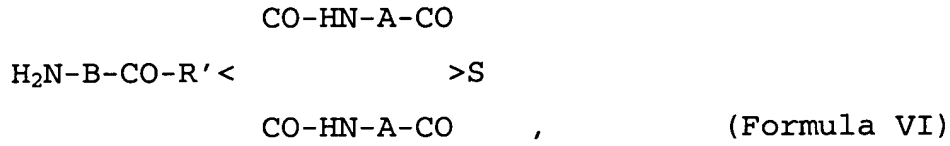
wherein, if N is present in R, X represents H, an Fmoc, Boc or Aloc group, and Y is OH or NH_2.

Claim 85 corresponds to cancelled claim 67, however Applicants have rewritten the claim to comport with the new steps defined in claim 84 and additionally added the product as defined by:



(Formula VI)

wherein B represents a peptide sequence, and R' represents a $N(CH_2-)_2$, NHCH<, or $NHCH(CH_2-)_2$ group. Claim 86 corresponds to cancelled claim 69, claim 87-89 correspond to cancelled claims 76-78. Claims 90-93 correspond to cancelled claims 80-83, and claims 94 and 95 correspond to cancelled claims 85 and 86. Support for these new claims can be found in the specification at pages 18-26, 33-34, and 44-63.

Conclusion

Accordingly, in view of the foregoing amendments and remarks, the Examiner is respectfully requested to reconsider and to allow the present claims in order to find this application to be in allowable condition.

Respectfully submitted,

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